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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,795	09/05/2001	Gunther Berndl	49727	4232

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 09/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,795	BERNDL ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Reconsideration filed June 30, 2005 and Translation of Foreign Priority Document to Prefect Priority filed July 11, 2005 is acknowledged. Claims 1-6 are pending in this application.

Claim Rejections - 35 USC § 112

The rejection of claims 1-6 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement are withdrawn in view of applicant's argument which are found to be persuasive.

Claim Rejections - 35 USC § 103

The rejection of claims 1-6 under 35 U.S.C. 103(a) as being unpatentable over WO 99/58529 to Meerpoel et al in view of Klimesch et al (4,880,585) is withdrawn in view of applicant's submission of the translation of the foreign priority document on 7/11/05, perfecting priority.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baert et al (6,365,188) in view of Stella et al (6,046,177) in further view of Murata et al (5,500,221).

Baert et al teach a solid mixture of cyclodextrin prepared via melt extrusion. The melt-extrusion mixture contains cyclodextrin and an active agent. See column 3, lines 26-40. Baert discloses that cyclodextrins increase the solubility of the insoluble drugs such as anti-fungals. Any suitable compound may be utilized provided that the drug does not decompose at high temperatures. See column 2, lines 45-60. Baert teaches melt-extrusion as the polymer extrusion technique wherein an active agent is embedded in one or more carriers. In this technique the active and excipients are molten in the extruder and hence embedded in the thermoplastic and thermomelting polymers. See column 3, lines 26-40. Additionally, the mixture may contain additives such as instant polyethylene glycol. See column 4, lines 34-42. The process includes a) mixing the cyclodextrin with the active agent and additives, b) heating the mixture until melting of one of the components occurs, c) forcing the mixture through one or more nozzles, and d) cooling the mixture to obtain a solid product. See column 4, lines 15-25. Although, a temperature of 239 degrees Celsius is exemplified, Baert discloses that different temperatures may be applied and discloses the method of ascertaining the required temperature. See column 5, lines 1-12. The extruder has counterotating screw with different shapes. See column 5. The melt-extruded mixture is preferably prepared without water or a solvent. The preferred ratio of the active to cyclodextrin is 1:3. See column 7, lines 64 to column 8, lines 4 and examples.

Baert et al do not teach the instant polymer binder in the extrusion mixture or the molecular weight of the PEG. Additionally, Baert does not teach the instant temperature of 220 degrees Celsius.

Stella et al teaches controlled release forms of solid formulations containing sulfoalkyl ether cyclodextrin (SAE-CD). The controlled release formulation contains a core containing an active agent, at least on SAE-CD, at least one rate controlling modifier, and at least one pharmaceutical acceptable excipient. See column 6, lines 1-7. The core may be made by several methods including melt extrusion. Note example 10. The release rate modifier provides either a delayed, sustained, timed, or targeted release of the active agent. See column 27, lines 40-50. Stella teaches varying the ratio of the rate controlling modifier and the drug such as 10:1 and 5:1, determines the release rate. The rate control modifier (exemplified HPMC) is varied from 25% to 50%. See column 17. Further, Stella teaches the use of binders such as celluloses, polyethylene glycols, polyvinylpyrrolidone, vinyl alcohol polymers, s in order to obtain suitable products. See column 27, lines 5-30. Some of the binders named also function as the release rate modifier. See column 27, lines 48-50. The binder is utilized in different proportions in different examples. Example 10 discloses a process utilizing melt extrusion wherein 2.5% of an active, 67.5% of SAE-CD, 10.5% PEG 6000, and excipients are melted at 60 degrees Celsius to form granules. Lastly, Stella et al disclose that major portion (lower limit 50% and preferably greater than 95%) of the SAE-CD is not complexed to the active agent (col. 12, lines 9-22).

Murata et al teach a sustained release suppository. Murata teaches the polymers that are utilized for adjusting the release rate of drugs are water-soluble polymers such as

hydroxypropylmethylcellulose (HPMC), polyvinylpyrrolidone, methylcellulose, etc. see column 3, lines 20-36.

It would have been obvious at the time the invention was made to combine the teachings of Baert et al, Stella et al, and Murata et al and utilize the instant water-soluble polymer PVP in the extrusion mixture of Baert et al. Firstly, one would have been motivated to do so since Stella teaches the use of a rate controlling modifiers, such as exemplified HPMC and teaches certain polymer binders among which instant PVP and PEG are taught, control the release rate of the active to provide for a delayed, targeted, sustained, etc. dosage form. Therefore, one would have been motivated to add a polymer such as instant polymer in the instant amount, to modify the release rate of the dosage form.

Secondly, one would have been further motivated to look to Murata and utilize instant PVP since Murata teaches the functional equivalency of Baert et al's exemplified rate-releasing modifier HPMC and instant PVP. Therefore, one would have been motivated to utilize the instant PVP with the expectation of similar results since the prior art teaches the functional equivalency of Stella's HPMC and PVP as polymers that adjust the release rate of drugs in a dosage form. Furthermore, Stella also states that the binders taught, among which PVP is taught, may also function as the rate controlling modifier; thus one would expect the instant PVP to act as a rate controlling modifier in Baert's dosage form.

Lastly, with regard to the temperatures, this is deemed to a manipulatable parameter that depends on the components and their melting point of each component. Further, Baert teaches that different temperatures may be applied and discloses the method of ascertaining the required temperature.

Response to Arguments

Applicant argues that the instant invention is directed to a fast releasing dosage form. Applicant argues that Stella teaches release modifiers but does not teach which binders act like release rate modifiers. Applicant argues that Stella does not specify the effect that can be attributed to the respective binder or release rate modifier. Applicant argues that Stella's example 10, which is viewed by as the closest prior art, only teaches slow release whereas instant invention has a fast release. Applicant argues that Stella teaches the superiority of sulfoalkylether cyclodextrins over hydroxypropyl-beta-cylcodextrin. Therefore, a skilled artisan would not want to replace SAE-cyclodextrin with a "standard" cyclodextrin.

Applicant's arguments filed 6/30/05 have been fully considered but they are not persuasive. Firstly, the examiner points out a substantial portion of applicant's arguments refer to the instant invention being a fast release dosage form. However, the examiner points out that the features (fast release) upon which applicant's arguments are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Secondly, the examiner points out that Stella teaches HPMC in a weight percent of 50% is taught as the release rate modifier. The examiner notes that HPMC is not part of applicant's recited species (c). Hence, the examiner relies on Murata to cure this deficiency. Murata teaches the polymers that adjust the release rate of drugs are water-soluble polymers such as Stella's hydroxypropylmethylcellulose (HPMC) and instant polyvinylpyrrolidone. Thus, Murata provides the motivation to further use instantly claimed PVP in light of Murata's teachings of functional

equivalency of HPMC and PVP. Additionally, the examiner notes that page 4 of instant disclosure states that HPMC may be used as a preferred binder. Therefore, the examiner suggests a showing of unexpected results, i.e. the criticality of the instant binders, to overcome the obviousness rejection.

With regard to example 10, the examiner points out that Stella teaches 12.5% of HPMC, 10.5% PEG 6000, the active agent, SAE-cyclodextrin. Stella teaches the use of binders to obtain a suitable product. Stella teaches PEG as a binder of choice. Stella's use of PEG 6000 in example 10 for instance, is 10.5% and applicant claims 15%. The examiner points out that applicant has not established the criticality of the instant ranges.

Lastly, it should be noted that the substituting Baert's "standard" cyclodextrin with Stella's SAE-cyclodextrin is not the premise of the examiner's rejection. The examiner's points out that the examiner is not stating that the motivation to look to Stella is to use SAE-cyclodextrin. The premise of the rejection is that a skilled artisan would have been motivated to look to Stella and Murta and utilize the instant polymers (PVP or PEG) for its release-rate modifying purposes. Therefore, this argument is moot.

For the reasons set forth, the rejection is maintained.

Conclusion

All the claims are rejected at this time.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616

SSG

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER